Management and Mitigation Strategies for Carfilzomib-Associated Side Effects

Hi, this is Sandy Kurtin, nurse practitioner from University of Arizona Cancer Center. We are going to talk about carfilzomib. Carfilzomib is a second-in-class irreversible proteasome inhibitor approved for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated relapsed or refractory disease. Relapsed or refractory disease is defined as disease progression on or within 60 days of completion of the last therapy. The Phase-II PX-171-003-A1 study established safety and efficacy of single-agent carfilzomib in the treatment of patients with relapsed and/or refractory multiple myeloma. The median number of prior lines of therapy in this population was five; 74% of patients had documented progression on their most recent line of therapy, all but one patient had received bortezomib and all patients had received an immunomodulatory agent; 73% of the patients were refractory to bortezomib; 80% were refractory or intolerant to both bortezomib and lenalidomide. The overall response rate in the heavily pre-treated population was 23.7%. For the response of evaluable patients, the median duration of response was 7.8 months. Patients meeting eligibility criteria for this trial are similar to those analyzed by Kumar, et al., where patients who were identified as refractory to bortezomib and either refractory, intolerant, or ineligible for an immunomodulatory therapy had an expected overall survival of 9 months once identified. Based on these data, carfilzomib was approved on July 20, 2012 for patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy. The most common treatment emergent adverse events reported were myelosuppression with cyclic thrombocytopenia, pneumonia, not surprising in this heavily treated multiple myeloma population, fatigue, and dyspnea. The standard protocol for administration is 20 mg/m² given IV over 2 to 10 minutes days 1, 2, 8, 9, 15, and 16 every 28 days for cycle 1 with 27 mg/m² administrated in cycle 2 and subsequent cycles using the same dosing schedule if cycle #1 is well tolerated. Pre-medication with 4 mg of dexamethasone before each dose of carfilzomib in cycle 1 and in subsequent cycles as needed is recommended to reduce the incidence of dyspnea. The administration of 250 to 500 mL of normal saline during cycle #1 of treatment should be considered for patients not at risk for fluid overload. No dose modifications are necessary for patients with renal impairment. Administration of carfilzomib to patients with significant cardiopulmonary disease should be used with caution. It is advised to avoid starting cycle 1 of treatment at the end of the week to allow outpatient follow up if needed. Importantly, treatment of emerging peripheral neuropathy is rare. Antiviral prophylaxis is recommended for all patients receiving proteasome inhibitor therapy. Carfilzomib is currently being evaluated in a number of trials using modified dosing or in combination with other novel agents. You can learn more about these trials at the Managing Myeloma website.

References:


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Kyprolis (carfilzomib) for injection. Highlights of Prescribing Information. Form 05-1088-00. Accessed at